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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
LANDSMAN, ROBERT S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,356	COCKS ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-9 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5-9 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Formal Matters

A. The Amendment dated 1/26/04 has been entered into the record.

B. Claims 1-19 were pending. Claims 3, 4 and 10-19 have been canceled and new claim 20 has been added. Therefore, claims 1, 5-9 and 20 are pending and are the subject of this Office Action.

C. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Specification

A. The objection to the specification has been withdrawn in view of Applicants' amendment which properly arrange the specification.

B. The specification remains objected to regarding the consistency of the Brief Description of the Figures. Applicants stated that they have amended this section of the specification. However, the brief description of figures with multiple parts should be labeled, for example, as "Figures 3A-3D show..." and "Figures 22A and B depict..." The brief descriptions of the following claims require this amendment: Figures 3A-3D, 5A and 5B, 8A-D, 15A and 15B, 16A-D, 19A-D, 20A-C, 22A and 22B, 26A-D, 27A-C, 28A and 28B, 29A-D, 32A-C, 33A-C and 38A-F.

C. The objection regarding page 29/41of the Figures has been withdrawn in view of Applicants' amendment changing Figure "27" instead of Figure "38."

D. The objection to the Figures regarding two Figures labeled "36" has been withdrawn in view of Applicants' amendment changing one Figure "36" to Figure "35."

E. The objection to the specification regarding the omission of an Abstract has been withdrawn in view of Applicants' submission of a proper Abstract.

F. The specification is objected to since Table 3 (page 65) is not in sequence compliance (see under "PAR3" and "PAR4." According to 37 CFR 1.821(d) (MPEP § 2422), where the description or claims of a patent application discuss a sequence listing that is set forth in the "Sequence Listing" in accordance

with paragraph (c) of this section, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. Sequences appear on page X, line Y, of the specification but are not identified by SEQ ID NO as required.

3. Claim Objections

A. The objection to claim 6 has been withdrawn in view of Applicants' amendment to recite the SEQ ID NOs instead of "SEQ ID NO:<400>."

4. Claim Rejections - 35 USC § 112, second paragraph

A. The rejection of claims 1-9 under 35 USC 112, second paragraph, has been withdrawn in view of Applicants amendment to claim 1 to remove the phrase "for a time." Dependent claims 3 and 4 have been cancelled.

B. Claim 1, 2 and 5-9 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a conclusion step in claim 1 which allows one practicing the claimed method to determine when the method has been completed. This step would include an identifiable endpoint, similar to that deleted by Applicants in the present amendment.

C. Claim 5 recites the limitation "airway disease condition" into claim 1. There is insufficient antecedent basis for this limitation in the claim.

D. Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a conclusion step in claim 1 which allows one practicing the claimed method to determine when the method has been completed. This step would include an identifiable endpoint.

5. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. Claims 1, 2 and 5-9 remain rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 4-5 of the Office Action dated 7/21/03. Applicants argue that they have amended claim 1 to recite "a method for a prophylaxis or a treatment of inflammation of an airway of an animal" and that they have amended claims 13 and 15 to recite, "inhibition of inflammation."

These arguments have been considered, but are not deemed persuasive. Applicants have not demonstrated that PAR2 is effective in preventing or treating all types of inflammation in the airway. Not only is the breadth excessive regarding all types of inflammation in all tissues in the airway, but Applicants have only provided guidance and working examples that agents which activate PAR2 can relax bronchial rings (see, for example, Figures 7-9). Relaxation of bronchial rings would help to prevent or alleviate bronchoconstriction, which, as the name implies, is a physical constriction of the bronchial rings. It is well-known in the art that bronchoconstriction is a distinct event from inflammation, such as asthma or hayfever, which involve the release of histamines and other agents which produce swelling of tissue. The mechanism of inflammation, which involves increased blood flow and the recruitment of immune cells to the area of inflammation, is distinct from bronchoconstriction, which is a muscular event and, therefore, does not require the presence of immune cells, or activation of the immune system. Applicants have not demonstrated that activation of PAR2 can affect inflammation, only bronchoconstriction. Therefore, it would not be predictable to the artisan that an agent which activates PAR2 to relax the bronchial rings would necessarily be able to reduce or prevent inflammation of the airways, which encompass more tissue than only the bronchial tube (e.g. alveoli). Furthermore, Applicants have not provided and guidance demonstrating that PAR2 are present in all airway tissues.

In addition, the breadth of the claims remains excessive with regard to Applicants claiming any and all "agents" (i.e. compositions) which can treat airway inflammation. The specification only demonstrates that TRAP an PAR2-AP can mediate bronchoconstriction via PAR2. The instant fact pattern is similar to that in *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), wherein a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification at most disclosed only those means known to the inventors. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See also *Fiers v. Sugano*, 984 F.2d 164, 25 USPQ2d 1601 (Fed. Cir. 1993), and MPEP § 2164.08(a). It is clear that there are compounds (i.e. agents) which are required for the PAR2 receptor activity. However, the claims fail

to recite any structural limitations, and thus the skilled artisan would have to resort to trial and error experimentation to identify compounds meeting the functional limitations of the claims, even though a suitable assay for PAR2 binding activity is disclosed.

Applicants also argue that they have amended claim 6 to remove the recitation of "functional equivalents, homologs or derivatives." However, claim 9 still recites "functional derivatives or homologs." Applicants have not provided any arguments as to why this limitation was not removed from the claims. Therefore, the arguments provided in the paragraph bridging pages 4-5 of the Office Action dated 7/21/03 remain.

In summary, the breadth of the claims is excessive with regard to Applicants claiming preventing and treating all types of airway inflammation. Applicants have only provided guidance and working examples of PAR2 activation to relax the bronchial rings and have not provided any guidance or working examples that PAR2 can prevent or treat inflammation. Due to the distinct mechanisms of muscle relaxation (bronchoconstriction) and inflammation, it would not be predictable to the artisan that activating PAR2, which is known to produce bronchoconstriction, would be effective in preventing or reducing inflammation. Similarly, the breadth of claim 9 is excessive regarding the use of "functional derivatives and homologs" of the TAT protein. Applicants have not provided any guidance or working examples of what amino acids can be altered and still produce a functional TAT protein, nor would it be predictable to the artisan which residues to alter to maintain this function. For these reasons, the Examiner maintains that undue experimentation is required to practice the claimed invention.

If Applicants believe they do have support for the use of PAR2 in inflammation, they are required to point out exactly where in the specification this support can be found. It is believed that all pertinent arguments have been addressed.

B. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of prophylaxis or treatment in an animal, does not reasonably provide enablement for these methods in a human. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence

of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Applicants have not provided any guidance or working examples that agents which are capable of treating inflammation in animals are able to treat inflammation in humans nor would it be predictable, in the absence of an art-accepted model, that treatment in animals is indicative of successful treatment in humans. Given this lack of guidance and working examples as well as lack of predictablity to the artisan how to treat these conditions in humans, the Examiner holds that undue experimentation is required to practice the invention as claimed.

6. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. **"Functional derivative or homologues"** of TAT would have one or more amino acid substitutions, deletions, insertions and/or additions to the TAT protein.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "TAT" alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

B. Claims 1, 2, 5-9 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. The claims recite "**agents capable of activating an airway epithelium PAR2**." Applicants have not provided adequate written description of any "agents" other than the proteins of SEQ ID NO:1, 2 and 3 (TRAP and PAR2-AP).

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1, 2 and 3 alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

7. Claim Rejections - 35 USC § 102

A. The rejection of claims 1, 5 and 6 under 35 USC 102 have been withdrawn in view of Applicants' amendments to the claims to recite "PAR2." Cicala do not teach the use of PAR2 in inflammatory conditions.

8. Claim Rejections - 35 USC § 103

A. The rejection of claims 1, 2 and 5-9 under 35 USC 103 have been withdrawn in view of Applicants' amendments to the claims to recite "PAR2." Cicala do not teach the use of PAR2 in inflammatory conditions, nor do they teach that PAR2 were present in airway epithelium.

9. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
March 31, 2004